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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO
09/820,320	03/28/2001	Henry E. Young	1304-1-019 CIP1	4118

7590 06/11/2003

KLAUBER & JACKSON
411 Hackensack Avenue
Hackensack, NJ 07601

EXAMINER
TON, THAIAN N

ART UNIT	PAPER NUMBER
1632	12

DATE MAILED: 06/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)	
09/820,320	YOUNG ET AL.	
Examiner	**Art Unit**	
Thai-An N. Ton	1632	

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *1-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Claims 1-32 are pending.

Claims 24-32 are under current examination.

Election/Restrictions

Applicant's election with traverse of Group VII [claims 24-32] in Paper No. 11 is acknowledged. The traversal is on the ground(s) that the groups designated by the Examiner fail to define compositions and methods, with properties so distinct, as to warrant separate examination and search. Applicants argue that the claims of Group I. which are drawn to pluripotent embryonic-like stem cells are fundamentally related to the methods of Group VII, which is drawn to methods of cellular transplantation. Applicants argue that the search for any of the methods separately classified would require an additional search of the identical classes, wherein the methods of Group I are classified, thus Applicants submit that the search and examination of the entire application, or at least Groups I and VII can be made without serious burden. See p. 3, 2nd ¶ of Applicants' response.

This is not found persuasive because the Examiner has clearly shown that the invention of Group I [directed to pluripotent embryonic-like stem cells, methods of isolating pluripotent embryonic-like stem cell lines] and the invention of Group VII [methods of cellular transplantation], are related as product and process of use; and that MPEP §806.05(h) states that:

A product and a process of using the product can be shown to be distinct inventions if either or both of the following can be shown: (A) the process of using as claimed can be practiced with another materially different product; or (B) the product as claimed can be used in a materially different process.

The Examiner has shown that the embryonic-like stem cells of Invention I can be used in a materially different process of using the product; that the embryonic-like stem cells of Invention I can be used to make transgenic animals.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention(s), there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 11.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Priority

Applicant has claimed priority to two U.S. Applications, 09/668,508, filed September 22, 2000 and 09/404,895, filed September 24, 1999. Applicant is

required to refer to all prior Applications in the first sentence of the specification, and update the status of each Application. See MPEP §201.11, 201.11(a) and 1893.03(c).

Specification

The disclosure is objected to because of the following informalities: pp. 113-114, there is a large blank area; furthermore, the sentences bridging pp. 113-114 do not make sense.

Page 234, Example 11, line 4 states *Abstract.* P. 255, line 30 states *Abstract.* Page 274, line 1 states *Abstract.* This is confusing, as there should be only one abstract per specification. Applicant is required to remove this language.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled

in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to methods of transplanting embryonic-like stem cells into a host. In further embodiments, the claims are directed to methods of preventing and/or treating cellular debilitations, derangements and/or dysfunctions, and/or other disease states in mammals by administration of a therapeutically effective amount of pluripotent embryonic-like stem cells, or cells or tissues derived therefrom; and pharmaceutical compositions for treatments of cellular debilitation, derangement and/or dysfunction in mammals.

The specification teaches pluripotent stem cells that can be used in methods of treatment, such as cell or tissue transplantation for the treatment or prevention of cellular debilitations, derangements, and/or dysfunctions and/or other disease states. See pp. 16-17, pp. 59-64, for example. The specification further teaches therapeutic compositions which comprise the claimed pluripotent stem cells, which would be used in the therapeutic methods. See pp. 67-69, for example. The specification teaches that DNA sequences of a gene or protein of interest may be transfected into the pluripotent embryonic-like stem cells of the invention and the resulting transfected cells can be used in methods of treatment. See pp. 73-75.

In particular, the specification teaches that muscle tissues were isolated from rat pups, human, rabbit, avian and mouse and cell cultures produced from the isolated tissues. The specification teaches that the cells were clongenically analyzed

and cultured and the cells were allowed to propagate past 50 cell doublings. Clones were isolated and allowed to propagate further and examined using insulin [a progression factor] and dexamethasone [a lineage-induction agent] to determine if the cells were lineage-committed progenitor cells or lineage uncommitted pluripotent cells. See Example 1. The specification further teaches that to isolate a population of pluripotent mesenchymal stem cells, cells were isolated from whole marrows of adult rats, cultured and treated with dexamethasone. The cells were then assayed for various phenotypes [e.g. mineralized tissue, cartilage, fat, muscle, smooth muscle, endothelial cells]. The specification teaches that the cells isolated from the bone marrow responded to the dexamethasone treatment by differentiating into various phenotypes in a manner identical to cells obtained from skeletal muscle and heart. See Example 2. The specification teaches that mesenchymal stem cells were isolated from rat granulation tissue, and that these cells were capable of differentiating into multiple phenotypes upon treatment with dexamethasone. See Example 3. Mesenchymal stem cells were isolated from adult human skeletal muscle, where it was found that these cells were capable of differentiation into various phenotypes [*e.g.*, mineralized tissue, cartilage, muscle, smooth muscle, endothelial cells, hematopoietic cells] upon treatment with dexamethasone. See Example 4.

The specification teaches the differentiation of 3T3 cells [a cell line derived from embryonic mouse tissue that appears fibroblastic] into multiple phenotypes

[adipocytes, chondrocytes, osteoblasts, smooth muscle, endothelial, skeletal myotubes] upon treatment with dexamethasone. See Example 5. Pluripotent stem cells were stimulated with various bioactive factors and the growth characteristics and phenotypic expression were analyzed. See Example 10 and Table 12. The specification teaches that postnatal pluripotent epiblastic-like rat stem cells were transfected with Lac-Z and processed for implantation. The cells were incubated with sterile foam gel which was then randomly implanted the necks of adult male out-bred Sprague-Dawley rats. The animals were then examined for five weeks. Necropsy results noted no inflammatory response in the animals. See Example 12. Postnatal human pluripotent stem cells were co-transplanted individually as naïve and hematopoietic induced stem cells, with murine hematopoietic stem cells into sublethally irradiated immune-deficient NOD/SCID mice. At 8 weeks post-transplant, the mice were sacrificed and the bone marrow, spleen and peripheral blood were analyzed for human cells using specific markers. All markers were negative except for Class I in the bone marrow, it was found that approximately 0.5% of the bone marrow contained human Class I positive cells. See Example 15. The specification further teaches that retroviral mediated gene transfer will be used to deliver genes to pluripotent stem cells which have been transplanted to immunodeficient scid/bg mice. This will allow tests of pluripotency of the transplanted cells and to monitor the behavior of the cells within normal and atrophied skeletal muscles. See Example 17.

The specification teaches that pluripotent stem cells which were transfected with Lac-Z were administered to a hind limb ischemic model in rat SCID animals. Particularly, the cells were administered by intravenous into the rat tail vein, or intramuscularly into the hind limb. β-gal positive cells were incorporated into the hind limb whether administered intravenously or intramuscularly. Additionally by IV injection, there was significant incorporation of β-gal positive cells in the bone marrow. See Example 18. The specification teaches that cardiomycocyte differentiation was studied in beta-galactosidase labeled rat postnatal pluripotent stem cell clones. The stem cells were injected into rat hearts and then analyzed for the implantation and differentiation of the stem cells. The specification teaches that a rat that received a cryogenic MI was injected with 200 μl of stem cells and its heart was harvested eleven days later and beta-gal positive cells were clearly seen, and integrated stem cells were found incorporated in the damaged myocardium. See Example 21. The specification teaches that transplants of the pluripotent stem cells were injected into the striatum of adult rats. The rats were then sacrificed one to two months after transplantation, and tissue sections of the striatum analyzed. See Example 23. The specification teaches that pluripotent stem cells were isolated from the skeletal muscle of adult male rabbits. These stem cells were then seeded into PGA felt. The discs were then incubated to permit cell adhesion and entrapment within the polymer scaffold. The PGA felt was then implanted in a defect, which was made by drilling in the center of the femoropatellar groove. The

animals were then sacrificed 26 post implantation, the histology and mechanical testing of the femur were analyzed. The specification teaches that defects that were treated with the felt that had been exposed to the stem cells for 24 hours had highly variable histology, and that some samples showed good fibrocartilage and subchondral bone throughout the defect. It was found that there was excellent integration of the tissue in the defect with the host cartilage. In contrast, the PGA felt that was treated with the pluripotent stem cells for 2 weeks *in vitro*, prior to transplantation, showed consistent regeneration. See Example 26. The specification teaches that the pluripotent stem cells were administered to a spinal cord injury site and analyzed for six weeks following the injury. See Example 27.

The claims, as broadly written, are directed to cellular transplantation of stem cells, the state of the art of which is unpredictable. For example, Zandstra *et al.* [**Ann. Rev. Biomed. Eng.**, 3:275-305, 2001] discuss utilizing stem cells for multiple biotechnological applications, such as therapeutic gene delivery. Zandstra states that, "Although the potential for producing novel cell-based products from stem cells is large, currently there are no effective technologically relevant methodologies for culturing stem cells, or for reproducibly stimulating them to differentiate into functional cells." [See p. 275, *Abstract*]. Further, Zandstra discuss that the utility of stem cells is limited because the culturing of stem cells, and directed differentiation has not been achieved because culture optimization techniques have not been optimized, and, "The development of bioprocesses for the

generation or *ex vivo* maintenance of stem cells and their derivatives is complicated by the biological properties of stem cells." [See p. 276, 2nd ¶].

The unpredictable state of the art of *ex vivo* stem cell gene therapy is further supported by Boheler and Fiszman [**Cells Tissues Organs** 165:237-245, 1999] who review the state of the art of *ex vivo* stem cell gene therapy and state that, "The recent description of human ES cells portend the eventual use of allogeneic *in vitro* differentiated cells for human therapy. This goal, however, is fraught with obstacles." [See p. 237, *Abstract*, 2nd column]. Boheler teach that the limitations and problems of *ex vivo* stem cell technology include that the cells be expandable *in vitro*, show proper integration of selection vectors in either targeted or inconsequential random genomic sites and have homogenous cell phenotypes [see p. 243, 1st column, 1st full ¶].

Prelle *et al.* [**Anat. Histol. Embryol.**, 31(3): 169-186, June 2002], discuss the state of the art of cell therapy utilizing pluripotent stem cells. They state that many factors affect stem cell transplantation, such as the screening of donor sources, cell morphology, cell-surface marker expression, tissue-specific enzymatic activity, and characteristic gene expression patterns. Furthermore, they state that:

> *Before transplantation, it is essential to demonstrate relevant biological activity of stem cell preparations, e.g. insulin release of islet-like cells, glycogen storage of hepatocyte-intended cells or synchronous contraction of cells used for the replacement or cardiomyocytes. Before using human stem cells in the clinic, the cells must be transplanted into animal models of human diseases which were created by chemical, surgical, immunological or gene*

> *targeting methods. Also, evidence for anatomical and functional integration, and even migration of stem cells should be provided.* See p. 181, 2nd column.

They conclude that, "All steps of this comprehensive strategy to assess human stem cell safety have to be considered before this encouraging and challenging technique can be transferred into routine therapy of various diseases." See p. 182, 1st column, last sentence.

Henningson *et al.* [**J. Allergy Clin. Immunol.**, 111(2):S745-S753, 2003] teach that, "Many questions still remain to be answered before stem cells are considered safe for clinical applications, as discussed previously. Furthermore, there is sufficient concern about origin and identification of cells to warrant the existence of a safety net composed of a set of safeguards for human stem cells to be used in clinical applications." They teach that these safeguards include the screening of donor cells, the standardization of practices and procedures to maintain the integrity, uniformity and reliability of stem cell preparations, the ability to gauge the purity of a cellular preparation by rigorous and quantitative identification of cell types within a heterogeneous population of differentiating human cells, and that the human stem cell preparations must be shown to possess relevant biological activity. See p. S751, 2nd column, 1st ¶.

Furthermore, Strom *et al.* [**Curr. Opin. Immunol.**, 14(5):601-605, October 2002] teach that stem cell-based therapies will probably be derived from allogeneic sources, and that one of the major requirements for widespread stem cell therapy

would require the production of large amounts of allogeneic cells which can then be administered to patients. See *Abstract*. Particularly, they state that the two major barriers to the idealized clinical deployment of stem cell-derived replacement therapy are a method to select and facilitate the expansion of a pure population of a desired cell type, and that the cells that are produced would need to be immune tolerant to be used in transplantation, as the daily immunosuppressive therapies currently available are unacceptable for these applications. See p. 601, 2nd column, 1st full ¶. Strom teach that overcoming the rejection of the transplanted stem cells is an important factor, and that the creation of immune tolerant cells would enable the use of stem-cell therapies [see pp. 603-604, bridging ¶].

The claims as broadly written are drawn to treatment of any disease utilizing pluripotent embryonic-like stem cells, by any mode of administration. However, the specification fails to provide teachings or guidance as to what levels or amounts of pluripotent embryonic-like stem cells would correspond to a therapeutic effect. Furthermore, as stated *supra*, the state of the art clearly teaches that it would be necessary to characterize the various biological activities of the stem cells, and ascertain that the preparations would be capable of the functions required [e.g., insulin releasing]. The specification broadly teaches uses for the claimed stem cells, however, does not provide teachings or guidance to show that the stem cells would be capable of functioning in an appropriate manner in an appropriate physiological setting. The working examples provided by the specification teach the injection and

implantation of the pluripotent stem cells, however, the specification fails to show that the implantation of the pluripotent stem cells results in cells that can function in a biologically relevant fashion and produce a therapeutic result. Furthermore, the specification fails to show that the transplantation of the claimed stem cells would not cause rejection in the recipient; which the state of the art clearly shows is a major obstacle in the success of stem cell therapy.

Furthermore, certain embodiments of the claimed invention are directed to gene therapy [see claim 26]; the state of the art of which is unpredictable. It is noted that numerous factors complicate somatic cell gene therapy with respect to predictably achieving levels and duration of gene expression, factors which have not been shown to be overcome by routine experimentation. Palù *et al.* (**J of Biotech**, 68:1-13, 1999) discuss new developments for gene therapy of human diseases. In particular, they state that, "Although gene transfer into humans has been demonstrated in several clinical trails, with more than 300 currently underway worldwide, there is still no single outcome that undoubtedly shows a consistent benefit for the patient." (See *Abstract*). Palù *et al.* state that the factors that must be optimized for effective gene therapy include better delivery systems specifically tailored to individual diseases, as well as providing a sustained expression of a therapeutic gene in the appropriate cells. Further, the main limitations to successful gene therapy include low transduction efficiency, poor targeting, and adverse host immune response that often determine a low and short-term

expression of the transgene (see p. 2, 2nd column, 1st paragraph). Palù *et al.* state that, "As it appears from this introduction there is neither an ideal vector nor a common strategy generally valid for all applications: most likely each vector system will have to be tailored to a specific disease." (See p. 3-4, bridging paragraph). Palù *et al.* discuss various methods to improve transduction efficiencies of viral and retroviral vectors. Palù *et al.* conclude that the main obstacle to the development of gene therapy remains the target and long-term regulation of expression of the transgene (see p. 10, 2nd column, 2nd paragraph) which requires the improvement of the currently existing vectors and delivery systems.

The unpredictability in the gene therapy art is further supported by Romano *et al.* (**Stem Cells** 18: 19-39, 2000), who review the state of the art of gene transfer. Romano *et al.* state that the effectiveness of gene therapy programs are still questioned, as concerns of safety of gene delivery has arisen, and that, "From this standpoint, despite the latest significant achievements reported in vector design, it is not possible to predict to what extent gene therapeutic interventions will be effective in patients, and in what time frame." (See *Abstract*, 2nd column, p. 20, col. 1-2 bridging paragraph). Romano *et al.* discuss various considerations of vector design which must be addressed before effective implementation of gene therapy protocols. These include factors such as improvement of transduction efficiency, gene delivery safety, the enhancing of targeting and specificity of vectors to avoid unpredictable side effects due to the ectopic expression of the transgene in normal

tissues, and the possibilities of regulating transgene expression (see p. 21). Romano *et al.* review the main gene delivery systems that are currently available and discuss the various disadvantages of their use in gene therapy (see Table 1, p. 23). Romano *et al.* conclude that, "The degree of vector development is still not sufficiently adequate to meet all the requirements for phase III clinical trials. The field of vector design has to address very difficult tasks from the standpoint of improvement of the transduction efficiency and safety precautions," and "The nature of the risks associated with gene therapy treatments must be established and minimized as much as possible, in order to have a more positive risk/benefit ratio in favor of intervention. When all the requirements for more effective gene delivery and safer therapeutic applications are met, gene transfer technology will become an accepted reality in the clinical setting." (See p. 31, *Conclusion*).

The specification fails to overcome the above-described unpredictabilities associated with gene therapy art. The claims as broadly written, read on both *ex vivo* gene therapy and transfection of pluripotent embryonic-like stem cells *in vivo*, post transplantation. However, the state of the art of gene therapy is such that it would not be predictable with regard to transduction efficiency, delivery and maintenance of gene expression, which would be required for therapy. The specification fails to teach levels of expression of any gene of interest necessary to show treatment of a disease. As such, with respect to the unpredictable nature of the gene therapy art, it would not be predictable if the transplantation of the

claimed transfected stem cells would express and maintain expression for duration sufficient to be considered therapeutic in a subject.

Note that the above-cited post-filing art clearly indicated an unpredictable status of gene therapy. Although specific vectors, promoters, genes and routes of administration may be, or might have been, effective for a specific disease which provides a specific therapeutic effect, gene therapy, as broad-based art, is clearly unpredictable in terms of achieving levels and durations of expression which would result in a therapeutic effect. As such, evidence pertaining to a specific vector, gene, promoter, route of administration, and therapeutic effect must be correlative to what is claimed, and in the instant application, a correlation and/or nexus cannot be drawn.

Note that the issue of *correlation* is dependent upon the state of the art at the time of the invention. MPEP §2164 discusses that if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which the claimed invention broadly pertains, there is a lack of predictability in the art. As such, what is known in the art provides evidence as to the question of predictability.

Accordingly, in view of the quantity of experimentation necessary to overcome the unpredictabilities associated with stem cell transplantation and gene therapy, the lack of direction or guidance provided by the specification to carry out stem cell therapy, as broadly claimed, for the treatment of any disease, the lack of direction or guidance provided by the specification to carry out gene therapy

utilizing transfected stem cells, for the treatment of any disease, involving any particular vector, promoter, route of administration and subject, the breadth of the claims directed to any particular vector, promoter, route of administration or subject, as well as the unpredictable and undeveloped state of the art of stem cell transplantation and gene therapy it would have required undue experimentation for one of skill in the art to make and/or use the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 24-32 as written, are unclear. The claims recite "embryonic-like" stem cells. The specification states that these cells are, "derived from non-embryonic or postnatal animal cells or tissue, are capable of differentiation to cells of endodermal, ectodermal, and mesodermal lineages." See p. 41, lines 15-25. However, this is not sufficient to define "embryonic-like", as it is unclear how these cells would be "embryonic-like", as they are derived from non-embryonic or postnatal animal cells/tissues.

Claim 26, as written, is incomplete. The claim recites a method of *in vivo* administration of a protein or gene of interest, but no clear and defined steps are recited in the independent claims. While minute details are not required in method claims, at least the basic steps must be recited in a positive, active fashion. See Ex Parte Erlich, 3 USPQ2d, p. 1011 (Bd. Pat. App. Int. 1986). For example, it is unclear how transfecting pluripotent embryonic-like stem cells would relate to the preamble, a method of *in vivo* administration of a protein or gene of interest, as there is no step of administration.

Claims 27-30, as written, are incomplete. The claims fail to relate to their preamble, as merely administering pluripotent embryonic-like stem cells, or cells or tissues derived therefrom would not result in the methods of prevention, tissue repair, or treatment as claimed. The claims require clear and defined steps.

Claims 27, 29, 31, as written, are vague. The claims recite "and/or" throughout the claims. "And/or" is vague because if the information following the phrase is intended to further limit or expand the claim. Claim 32 depends from claim 28.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 24-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Kiem *et al.* [Blood, 92(6):1878-1886, September 15,8].

The claims are directed methods of transplanting pluripotent embryonic-like stem cells into a host, methods of treating or preventing cellular debilitations, deranges, and/or dysfunctions and/or other disease states in mammals by administration of pluripotent embryonic-like stem cells, or cells or tissues derived therefrom, and in further embodiments, the stem cells are transfected with a vector comprising a DNA or RNA which expresses a protein or gene of interest, and pharmaceutical compositions for the treatment of cellular debilitations, derangements and/or dysfunction in mammals, wherein the pharmaceutical composition further comprises a proliferation factor or a lineage-commitment factor

Kiem teach that baboon hematopoietic stem cells [HSCs] were harvested after *in vivo* priming using stem cell factor and granulocyte colony-stimulating factor. The HSCs were then transfected with a GALV-pseudotype vector which carries a gene a gene encoding human placental alkaline phosphatase. The expression of humantal alkaline phosphatase was then analyzed. See p. 1879, *Materials and Methods.* Five baboons were then transplanted with the transduced primed CD34-enriched marrow cells and DNA from the peripheral blood and marrow were analyzed for the presence of the vector sequences. See p. 1880, 2nd column and Tables 1-2.

Accordingly, Kiem teach the claimed invention.

Claims 27-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang *et al.* [**Transplantation**, 65(2):188-192, January 1998].

The claims are directed to methods of preventing and/or treating cellular debilitations, derangements and/or dysfunctions and/or other disease states in mammals, comprising administering to a mammal a therapeutically effective amount of pluripotent embryonic-like stem cells, or cells or tissues derived therefrom, and methods of tissue repair or transplantation in mammals comprising administering to a mammal a therapeutically effective amount of pluripotent embryonic-like stem cells, or cells or tissues derived therefrom, and pharmaceutical compositions for such treatments.

Wang teach rats were transplanted with liver, pancreas, heart and kidney allografts [see *Materials and Methods*]. It was found that liver allografts were spontaneously accepted, whereas the pancreas, heart and kidney allografts were rejected. Note that the claims are directed to "pluripotent embryonic-like stem cells, or *cells or tissues derived therefrom.*" Accordingly, the allografts, as taught by Wang, would be considered cells or tissues derived from pluripotent embryonic-like stem cells.

Accordingly, Wang anticipate the claimed invention.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thái-An N. Ton whose telephone number is (703) 305-1019. The examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the examiner be unavailable, inquiries should be directed to Deborah Reynolds, Supervisory Primary Examiner of Art Unit 1632, at (703) 305-4051. Any administrative or procedural questions should be directed to William Phillips, Patent Analyst, at (703) 305-3482. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Deborah Crouch

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP ~~1800~~ 1630

TNT

Thái-An N. Ton
Patent Examiner
Group 1632